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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,684	04/23/2001	Parkash S. Gill	017986-000420US	7332

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/743,684	GILL, PARKASH S.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,10,11,17-23,29-34,36-49,51,52 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7* is/are allowed.

6)☒ Claim(s) *6,10,11,17-23,29-34,36-49,51,52 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/31/2007 has been entered.

2. The amendment filed 1/31/2007 is acknowledged. Claims 24-28, 53 and 54 were canceled. Claim 55 was added.

Claims 6, 7, 10, 11, 17-23, 29-34, 36-49, 51, 52 and 55 are examined on the merits.

3. The copy of the 1449 of the IDS originally submitted Jan. 29, 2003 is acknowledged. Because the copy is of the marked up 1449, the examiner is listing these references on an 892, so that these references will appear on the front face of the patent, should a patent issue from this application.

Claim Rejections Withdrawn:

4. The objection to claim 23 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in view of the amendment.

5. The rejection of claims 7 and 54 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

6. The rejection of claim 54 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment canceling claim 54.

7. The rejection of claim 53 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment canceling claim 53.

8. The rejection of claim 7 under 35 U.S.C. 102(e) as being anticipated by Hammerstedt (U.S. Patent 5,910,568; issued June 8, 1999; effective filing date Jan. 11, 1996; cited in the IDS) is withdrawn in view of the amendment. Hammerstedt's polypeptide does not being with amino acids 2-6 of SEQ ID NO: 2. Therefore, Hammerstedt fails to anticipate the claim.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 6,10, 11, 17-23, 29-34, 36-49, 51, 52 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is indefinite because the definitions of Aa1, Aa2, Aa3 and Aa4 are unclear. These definitions are unclear because of the use of "or" between the definition of Aa4 and Aa5. Replacement of "or" with "and" is suggested.

Claim 23 is indefinite because the definition of "R" is unclear. In the first case "R" is defined as "Gln-Pro-Lys-Asp-Asn" (which is clear), but in the cases following, only "X" and/ "R'" (R prime) are defined. Therefore, it is not clear if "R" remains as defined for the first case, if "R" reverts back to the "R" as broadly defined in claim 11, from which claim 23 depends. The same situation arises for "X", which is clearly defined in the first and second cases, but not in the remaining cases.

Claim Objections

10. Claim 55 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 55 fails to further limit claim 11 because claim 55 includes SEQ ID NO: 19, which is a sequence that is out of the scope of sequences encompassed by claim 11. Claim 55 includes within its scope SEQ ID NO: 19, which is a sequence that starts with "GDVCQD", whereas claim 11 does not allow for sequences that start with "GDVCQD", because when R is absent, X (in this case "G") is absent.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 23 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment of claim 23 introduces new matter into the specification as originally filed.

Claim 23 is drawn to a peptide of claim 11. Claim 11 is drawn to an isolated polypeptide consisting of the sequence R-XDVCQD-R', wherein R is selected from the group consisting of Aa1-Aa2-Aa3-Aa4-Aa5, Aa2-Aa3-Aa4-Aa5, Aa3-Aa4-Aa5, Aa4-Aa5 and Aa5, or is absent; wherein Aa1 is glutamine, Aa2 is proline, Aa3 is lysine, Aa4 is aspartic acid or Aa5 is asparagines; wherein X is glycine, alanine, serine and threonine or is absent when R is absent; and R' is from 0 – about 59 contiguous amino acids. C"begins with Cys-Ile-Gln-Val (SEQ ID NO: 61)"laim 23 appears to be drawn in part to peptides where R and X are fully defined, but R' is defined as "begins with Cys-Ile-Gln-Val (SEQ ID NO: 61)", or in part to peptides where X is fully defined and R' is defined as "begins with Cys-Ile-Gln-Met-Val (SEQ ID NO: 62)", or in part to peptides where R' is defined as "begins with Cys-Ile-Gln-Met-Val (SEQ ID NO: 62)", "begins with Cys-Ile-Gln-Met (SEQ ID NO: 63)", "begins with Cys-Ile-Gln-", "begins with Cys-Ile", or "begins with Cys".

The support provided by the specification is insufficient to support the subgenuses of peptides that appear to be defined by claim 23 (with the exception of "begins with Cys", which is supported by original claim 18). The original claims fail to provide any support for the new

subgenuses. The specification provides one example of a peptide that falls within the scope of each of the new subgenuses defined by claim 23. The specification provides peptides where the R' *is* Cys-Ile-Gln-Met-Val (SEQ ID NO: 62), Cys-Ile-Gln-Met (SEQ ID NO: 63), Cys-Ile-Gln-, or Cys-Ile, *and* where R is absent *and* X is absent. However, these examples are not representative of the new subgenuses of peptides, because as claim 23 is currently set forth, it appears that R is defined by claim 11 and that any residue may be added after the R' up to the size limit of 59 amino acids. Thus, claim 23 defines subgenuses and not individual peptide sequences. There does not appear to be any teachings in the specification to indicate that these subgenuses were originally contemplated, and applicants have not indicated in the remarks accompanying the amendment where in the specification support may be found for contemplation of these subgenuses.

12. Claims 45-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated fusion proteins where said fusion protein comprises the isolated polypeptide of claim 11 and cell targeting moiety, does not reasonably provide enablement for isolated fusion proteins where said fusion protein comprises the isolated polypeptide of claim 11 and a cytotoxic moiety. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is that the specification provides enablement for how to use a fusion protein comprising the isolated polypeptide of claim 11 and a cell targeting moiety, but does not provide enablement for how to use a fusion protein comprising the isolated polypeptide of claim 11 and a cytotoxic moiety, because the specification

fails to provide sufficient evidence that the polypeptides of claim 11 have a differential cell targeting function.

Claims 45-49 are drawn to isolated fusion proteins comprising the isolated polypeptides of claim 11 and a cytotoxic moiety, wherein the cytotoxic moiety and the polypeptide have functional activity independent of each other. Therefore, the intended use of the claimed isolated fusion proteins of claims 45-59 appears to be to selectively kill cells. The specification also teaches that because of the effect of the saposin B polypeptides (the part of the claimed fusion polypeptides that corresponds to the isolated polypeptide of claim 11) on specific cell types that the polypeptides can be used in conjunction with cytotoxic moieties to selectively kill certain cell types (see page 20, lines 10-14).

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The specification prophetically contemplates making and using fusion polypeptides where one part of the fusion polypeptide is a Saposin B polypeptide fragment and the other part of the fusion polypeptide is a cytotoxic moiety. However, the specification lacks any working embodiments demonstrating selective targeting of cells where some cell types are selectively killed with a fusion protein encompassed by claims 45-49. The specification does demonstrate in vitro that while peptides consisting of the amino acid sequences of SEQ ID NOS: 21 or 22

reduce cell proliferation of activated endothelial cells (KS Y-1 cells, Table 4), that these peptides do not reduce, to the same extent, cell proliferation of fibroblast cells (Table 5). However, this demonstration is insufficient to show that any Saposin B peptide may be used as a targeting moiety (as contemplated for claims 45-49), because this demonstration does not show that these peptides are not internalized by fibroblast cells, but instead, merely demonstrates that these peptides do not affect cell proliferation of fibroblast cells. There are no teachings in the specification or the prior art concerning the mechanism for the effect of Saposin B peptides on the proliferation of endothelial cells. Therefore, it is possible that the peptides of SEQ ID NOS: 21 and 22 are able to be internalized by all cell types, but that once internalized, only some cell types respond to them with a reduction in cell proliferation. There are examples in the art demonstrating the cytotoxic effect of a peptide is not due to exclusion by the cell membrane, but instead is due to a differential processing within a cell. For example, multimeric alpha-Lactalbumin enters both tumor cells and non-tumor cells, but is toxic only to tumor cells (see Hakansson, A., et al. Experimental Cell Research, 246: 451-460, 1999, page 453-454 and page 457). Thus, a differential effect on cell proliferation is not evidence that the peptides of SEQ ID NOS: 21 or 22 are excluded from fibroblasts, and therefore, is not evidence that peptides such as those of SEQ ID NOS: 21 or 22 could be used to selectively target a cytotoxic agent to endothelial cells.

In view of the lack of guidance provided by the specification, and further in view of the fact that differences in internal cellular processing of peptides may be responsible for the differences in susceptibility of endothelial cells compared with fibroblasts to the Saposin B peptides of SEQ ID NO: 21 or 22, the specification fails to provide guidance for how to use

Saposin B polypeptides as moieties to selectively target cytotoxic moieties to endothelial cells for the purpose of inhibiting angiogenesis. Therefore, one of skill in the art would not know how to use the fusion polypeptides of claims 45-49 in the methods contemplated in the specification.

Conclusion

Claim 7 is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
March 25, 2007

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SUPERVISORY PATENT EXAMINER